

Priority 11/5/98

Clean copy of pending claims  
64-95 and 105-108

64. A process for producing a long-term culture of immature dendritic cells, which process comprises:

- (i) providing a population of embryonic stem cells;
- (ii) culturing the embryonic stem cells in the presence of a cytokine or combination of cytokines which bring about differentiation of the embryonic stem cells into immature dendritic cells, whose protracted longevity and capacity for self-renewal [to] produce a long-term culture of immature dendritic cells; and
- (iii) recovering immature dendritic cells from the culture, which immature dendritic cells are capable of maturation to an immunostimulatory phenotype.

65. The process of claim 64 further comprising the step (iv) of inducing [stimulating] the immature dendritic cells to mature thereby producing mature immunostimulatory dendritic cells.

66. The process of claim 65 wherein the immature dendritic cells are stimulated to mature with an inflammatory mediator.

67. The process of claim 65 wherein the inflammatory mediator is LPS.

68. The process according to claim 64, wherein the cytokine or combination of cytokines is or includes IL-3.

69. The [he] process according to claim 68, wherein a combination of cytokines including IL-3 and GM-CSF is used.

70. The process according to claim 64, wherein the embryonic stem cells in (i) are in the form of embryoid bodies, generated by culturing purified embryonic stem cells in suspension for 14 days in the absence of recombinant leukemia inhibitory factor.

71. The process according to claim 64, wherein the embryonic stem cells are genetically modified.

72. The process of claim 71, wherein the cells express one or more heterologous gene(s).
73. The process of claim 72, wherein the one or more heterologous gene(s) encode a protein that has an immunomodulatory effect.
74. The process of claim 73, wherein the protein is a cell surface receptor.
75. The process of claim 74, wherein the protein is Fas-ligand.
76. The process of claim 72, wherein the one or more heterologous gene(s) express a dominant negative form of an endogenous protein.
77. The process of claim 73, wherein the protein is an antigen target for the immune system, such as an autoantigen, a tumor antigen, or a foreign antigen.
78. The process of claim 64, wherein the cell co-expresses two or more heterologous genes.
79. The process of claim 78, wherein one of the heterologous genes prolongs the life-span of the cell.
80. The process of claim 79, wherein the gene is an anti-apoptotic gene.
81. The process of claim 78, wherein the gene encodes FLIP or bcl-2.
82. The process of claim 64, in which one or more endogenous gene(s) have been inactivated.
83. The process of claim 82, wherein the inactivated endogenous gene(s) comprise any of: B7-1, IL-12, and the p35 or p40 subunit of IL-12.
84. The process of claim 71, wherein the embryonic stem cells are transfected with at least one gene which is expressed in the dendritic cells.

85. The process of claim 84, wherein the gene is under the control of a promoter which initiates or upregulates gene expression on maturation of dendritic cells.

86. The process of claim 84, wherein the gene is a reporter gene which expresses a detectable product in the dendritic cells.

87. The process of claim 86, wherein the gene encodes a fluorescent product.

88. The process of claim 87, wherein the gene is the GFP gene.

89. The process of claim 71, wherein the ES cells are genetically modified so as to inactivate at least one copy of at least one gene.

90. The process of claim 64, wherein the recovered immature dendritic cells are substantially pure.

91. The process of claim 64, wherein the cells are lymphoid.

92. The process of claim 64, wherein the cells are myeloid.

93. The process of claim 64, wherein the cells are human.

94. The process of claim 64, wherein the ES cells are derived from a mouse strain such as CBA/Ca or C57Bl/6.

95. The process of claim 94, wherein the ES cells are from the ESF116 cell line.

105. The process of claim 79 wherein the gene encodes FLIP or bcl-2.

106. The process of claim 85, wherein the gene is a reporter gene which expresses a detectable product in the dendritic cells.

107. The process of claim 106, wherein the gene encodes a fluorescent product.

108. The process of claim 107, wherein the gene is the GFP gene.